

DETAILED ACTION

Applicant's election with traverse of group XII (claim 61) in the reply filed on 12/13/2007 is acknowledged. The traversal is on the ground(s) that searching more than one of the groups (for example VIII and XII) set forth by the Office would pose no serious burden on the Examiner and Applicant also argues that SEQ ID NOS: 43, 45, 47 and 49 can be searched together (page 3 of remarks).

These have been considered, but not found persuasive. First, invention groups are different in method steps, method objectives, and/or materials used for performing the method. For example, group VIII, drawn to a method of screening for anticancer activity comprising contacting an anticancer drug to a cell, which requires a method step of screening a candidate anticancer drug and objective is finding a drug having the anticancer activity. However, the elected group XII, drawn to a method of diagnosing cancer by detecting the gene expression of cancer associated gene, which is based on the levels of the expression of a specific gene to determine whether the patient has a cancer or not. Searching the gene expression and a screening anticancer drug are not coextensive, which would impose a burden on the Examiner in the process of examination. Thus, the requirement is deemed proper as stated in MPEP, "Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects" (MPEP § 806.04, MPEP § 808.01). Second, as discussed in the requirement of election/restriction, the sequences of SEQ ID NOS: 43, 45, 47 and 49, although are homologous and related with cancer, each is unique and separately patentable sequence requiring a unique search of the prior art. Searching all of the sequences or more than one unrelated SEQ ID NO in a single patent application would constitute an undue search burden on the Examiner and the USPTO's resources because of the non-coextensive nature of these searches. For the reasons above, the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL**.

Claims 1-49, 52, 64, and 66-69 are cancelled.

Claims 74-97 are added. The newly added claims contain non-elected subject matter. During a telephone conversation with Mr. Gwilym John Owen Attwell on February 20, 2008, claims 82 and 83, drawn to a method of diagnosing cancer by determining the levels of protein with antibody, are withdrawn

Art Unit: 1643

from consideration and the newly added claims comprising claims 74-81 and 84-97 together with original claim 61 are examined for the method of detecting the nucleotides of SEQ ID NO: 43 (mRNA), NOT the protein or polypeptide. During the conversation, Applicant also elects breast cancer as a species of cancers in the response to the requirement of election of species. Affirmation of these election and withdrawal must be made by Applicant in replying to this Office action.

Thus, claims 50, 51, 53-63, 65, 70-97 are pending. Claims 50, 51, 53-60, 62, 63, 65, 70-73, 82 and 83 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 61, 74-81, and 84-97, drawn to a method for diagnosing cancer comprising determining the level of expression of very low lipoprotein receptor (VLDLR) mRNA of SEQ ID NO: 43 to the extent of breast cancer, are examined on the merits.

Specification

Specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 51 or paragraph [0149], which is improper incorporation by reference. Applicant is required to check entire specification and delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: non-initialed and/or non-dated alterations of the inventor, David W. Morris, have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Rejections - 35 USC § 112

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

Art Unit: 1643

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description- Method comprising detecting the variants of SEQ ID NO: 43:

Claims 61, 74-76, 78-81, 84-88, and 90-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted although low density lipoprotein receptor (VLDLR) is a well known family of proteins with two identified splicing variants VLDLRI and VLDLRII different in the presence or absence of exon 16, the term, VLDLR, recited in the methods of independent claims 74 and 79 are interpreted as comprising the variants of VLDLR having not been described either in the art or in this specification because the dependent claims, for instance, claims 61, 75, 87, claim a variant having a nucleotide sequences at least 95% identity to the SEQ ID NO: 43. Claims 74 and 79 are included here in this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession may be shown, for example, for the product claims by providing sufficient distinguishing identifying characteristics of the genus that include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, for the method claims, by describing an actual reduction to practice of the claimed invention. A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.

It is not the case here. Claims are drawn to a method for diagnosing cancer comprising determining and comparing the levels of an expression product comprising a nucleotide sequence of very low density lipoprotein receptor (VLDLR) mRNA or a gene product having at least 95% or 98% sequence

Art Unit: 1643

identity to or comprising a nucleotide sequence of SEQ ID NO: 43, complement or the homologous identified by hybridization in the breast cancer samples to the normal control samples. Thus, the claimed methods are inclusive of a genus of variants comprising addition, deletion, and/or substitution of VLDLR having 95% or 98% identity to SEQ ID NO: 43 that could be hybridized. However, the instant specification fails to describe enough species of the polynucleotide, complement or VLDLR mRNA comprising or having 95% or 98% sequence identity to the polynucleotide of SEQ ID NO: 43, which are detected and could be used for diagnosing breast cancer. It is also noted that "a nucleotide sequence" (claim 61, 90 etc.) and "a sequence" (claim 94 etc.) read on as small as few nucleic acid residues and "a polynucleotide that hybridized to a nucleotide sequence of SEQ ID NO: 43" (claim 90) reads on a fragment of SEQ ID NO: 43. Thus, there is no showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claims and determined that the invention would work for its intended purpose.

The specification contemplates a method of detecting a cancer associated with expression of a polypeptide in the test cancer by detecting the level of product of cancer associated (CA) genes in the test sample (page 7-8) and lists over 200 CA genes and the encoding proteins. The specification teaches the VLDLR mRNA corresponding to the nucleotide sequence of SEQ ID NO: 43, encoding a protein of SEQ ID NO: 44 (page 104, 111, table 17) and briefly states the protein as a cancer associated protein (CAP) expressed on a cell surface (page 141). The specification, in the examples, describes the well known method of detecting the gene expressions of the CA in the cancer cells or tissues by RT-PCR and ELISA etc. However, the specification does not teach representative numbers of the variants of SEQ ID NO: 43 including the addition, deletion, or substitution having at least 95% or 98% sequence identity or detection of the variants in the breast cancer condition. Thus, the specification fails to provide adequate written description for the instantly claimed invention.

The state of the art has described two VLDLR variants (VLDLR-I and VLDLR-II). The difference between two receptors is lack of 84 nucleotides that encodes the domain with potential O-linked glycosylation (exon 16) in VLDLR-II (Martensen et al., Eur. J. Biochem vol 248, page 583-591, 1997). The

Art Unit: 1643

cDNA, or mRNA of SEQ ID NO: 43 disclosed in the instant specification encodes the second VLDLR-II without exon 16 as evidenced by the sequence search result. Martensen et al., also teach that the VLDLR-II without exon 16 is the main or only variant expressed in the breast cancer. As such, the art of record has not identified other variants of VLDLR or the gene expression products having at least 95% identity to SEQ ID NO: 43 that is upregulated in the breast cancer cells or tissues and no teaching or suggestion in the record of the art on the mutation or substitution of the gene product with 95% or 98% identity to the DNA of SEQ ID NO: 43 in the breast cancer development or cancer condition has been recorded.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. The claimed methods require detecting the levels of expression of SEQ ID NO: 43 or its homologous variants for detecting a breast cancer. Without showing the enough teaching of differential expression of the species of genes or gene products in the cancer patient samples, the skilled artisan cannot practice the claimed method for the cancer diagnosis and therefore conception is not achieved until reduction to practice has occurred. Accordingly, one skilled in the art would not recognize from the specification that the applicants were in possession of the claimed methods at the time the application was filed.

Lack of description of the instant specification and the record of the art, only the method of detecting a breast cancer by determining and comparing the levels of the gene product, mRNA, of SEQ ID NO: 43, not the variants having 95% or 98% sequence identity to a sequence of SEQ ID NO: 43 meet the written description provision of 35 U.S.C. §112, first paragraph.

Art Unit: 1643

Applicant has been directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Also, see MPEP 2163.

Scope of Enablement

Claims 61, 74-76, 78-81, 84-88, and 90-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing breast cancer comprising determining and comparing the levels of the nucleotide sequence of SEQ ID NO: 43 and a method of detecting one variant of VLDLR disclosed in the art (see art rejection below), does not reasonably provide enablement for the method of detecting a cancer comprising breast cancer by determining and comparing the levels of the variants of VLDLR or any nucleotides having at least 95% or 98% sequence identity to SEQ ID NO: 43. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of necessary experimentation claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands*, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir.1988).

Claims are broadly drawn to a method for diagnosing cancer comprising determining and comparing the levels of an expression product comprising a nucleotide sequence of very low density lipoprotein receptor (VLDLR) mRNA or a gene product having at least 95% or 98% sequence identity to or comprising a nucleotide sequence of SEQ ID NO: 43, complement or the homologous identified by hybridization in the breast cancer samples to the normal control samples.

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The method objective of claims is diagnosing cancer by determining the expression level of SEQ ID NO: 43 and its variants. Thus, it would be expected that one of skill in the art would be able to use the method without undue a quantity of experimentations.

Art Unit: 1643

The specification teaches the VLDLR mRNA of SEQ ID NO: 43, encoding a protein of SEQ ID NO: 44 (page 104, 111, table 17) and briefly states the protein as a cancer associated protein (CAP) expressed on a cell surface (page 141). The specification contemplates a method of detecting a cancer associated with expression of a polypeptide in the test cancer by detecting the level of product of cancer associated (CA) genes in the test sample (page 7-8) and lists over 200 CA genes and the encoding proteins. The specification teaches few variants of SEQ ID NO: 43 with several nucleotide difference in C-terminal untranslated region, for example SEQ ID NO: 47, 51 etc. may also associated with cancer (see search result of SEQ ID NO: 43 in SCORE), the specification does not teach other variants of SEQ ID NO: 43 that contains an addition, deletion, or substitution at coding region having at least 95% or 98% sequence identity to the SEQ ID NO: 43 which are differentially expressed in the breast cancer condition. The specification does not provide an enabled disclosure for one skilled in the art to make or use broadly claimed invention without undue a quantity of experimentation.

The state of the art has described two human VLDLR variants (VLDLR-I and VLDLR-II). The difference between two receptors is lack of 84 nucleotides that encodes the domain with potential O-linked glycosylation (exon 16) in VLDLR-II and only the VLDLR without the exon 16 is overexpressed in the breast cancer patients (Martensen et al., Eur. J. Biochem vol 248, page 583-591, 1997, see the art rejection below). As such, one skilled in the art clearly knows that not all VLDLR variant are involved cancer or breast cancer condition or contribute for the cancer development.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that method as broadly claimed would function as broadly claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention

Claim Rejections - 35 USC § 102

Art Unit: 1643

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 61, 74-81, 84-90, and 93-97 are rejected under 35 U.S.C. 102(b) as being anticipated by Martensen et al., (Eur. J. Biochem. vol 248, page 583-591, 1997) as evidenced by sequence search results.

Claims are drawn to a method for diagnosing cancer comprising determining and comparing the levels of an expression product comprising a nucleotide sequence of very low density lipoprotein receptor (VLDLR) mRNA or a gene product having at least 95% or 98% sequence identity to or comprising a nucleotide sequence of SEQ ID NO: 43, complement or the homologous identified by hybridization in the breast cancer patient samples to the normal control samples, wherein the VLDLR binds to LDL, wherein the different (increase) expression of VLDLR compared to the normal tissues or control indicates breast cancer.

It is noted that PCR reaction is considered as comprising the step of hybridization.

Martensen et al., disclose a method which would be used for diagnosing a breast cancer by determining the levels of expression of VLDLR. Martensen et al., first disclose two human VLDLR variants VLDLR-I and VLDLR-II and disclose that difference between two receptors is lack of 84 nucleotides that encodes the domain with potential O-linked glycosylation (exon 16) of VLDLR-II (page 584, col 1). Martensen et al., cite a reference of Webb et al., (page 584, col 1, para 1, and page 591, col 2, reference No.9), who disclose the sequence of VLDLR, which is encoded by the SEQ ID NO: 43 of instant claims as evidenced by the sequence search result (attached, page 1, Webb et al., highlight). The cDNA, or mRNA of SEQ ID NO: 43 recited in the claims encodes the second VLDLR-II without exon 16

Art Unit: 1643

as evidenced by the sequence search result (attached). Martensen et al., disclose RT-PCR for detecting the differential gene expression of VLDLRs comprising contacting and hybridizing the polynucleotide (primers) to determine the expression of gene product in the breast cell lines and carcinoma tissue samples compared to the normal cells or tissues and also disclose that the primers are designed specifically to recognize the gene product of VLDLR I and II that would form a duplex in the PCR reactions (figure 1 and 5, page 585-6). Martensen et al., further disclose that binding VLDLR to its ligand, lipoprotein (page 583, col 1 and page 588, col 1). Since claimed method is not drawn to a specific oligonucleotide as primers or a probe for the hybridization or RT-PCR, the method of Martensen et al., would detect the nucleotide sequence having at least 95% identity to the sequence of SEQ ID NO: 43 or its full complement (page 586, col 2) and would anticipate the claimed method.

Since the limitation of highly stringent condition recited in claim 90 is not further defined in the claims, the limitation of hybridization (annealing) at 50 °C is not distinguished from the prior art.

The method of prior art appears to meet the requirements of the instant claims regarding the expression of VLDLR mRNA comprising the sequence SEQ ID NO: 43 in a breast cancer patient because the references comprising Webb et al., cited by Martensen et al., teach the amino acid sequences VLDLRs which is encoded by the instant mRNA of SEQ ID NO: 43. However, regarding the sequence alignment or identity between VLDLR mRNA of Martensen et al., and VLDLR mRNA of SEQ ID NO: 43 in the instant application, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

In addition, for this rejection, the phrase "wherein, an increase of at least 50%, 100%, 200% etc. from the levels of the mRNA in the breast patients sample relative to normal control" recited in the claims are not considered as an active method step. The wherein clause is interpreted as a mental step.

Art Unit: 1643

2. Claims 61, 74-81, 84, 86-89 and 94-97 are rejected under 35 U.S.C. 102(a) or 102(e) as being anticipated by Hopkins et al., (US Application Publication, 2002/0137077, filing 10/25/2001).

The claims are set forth above.

Hopkins et al., disclose a method for diagnosing cancer by determining the levels of expression of VLDLR or the gene product of SEQ ID NO: 43. Hopkins et al., first disclose the nucleotide sequence having 3622 nucleic acids (cDNA, #5, or SEQ ID NO: 5, table 1, page 16) encoding very low density lipoprotein (VLDLR) which is up-regulated (two fold) and can be used for diagnosing cancer [0012]. The cDNA, #5 of Hopkins et al., is 96.2% local similarity to the VLDLR of SEQ ID NO: 43 as evidenced by the sequence search result in database RNG (attached), which would bind to its ligand lipoprotein (LDL). Hopkins et al., disclose the method step of nucleotide hybridization to detect the hybridization complex and determine the expression of gene product from the cDNA prepared from the cell lines and tissue samples of patients compared to the normal or control cell or tissues [0013, 0054]. Hopkins et al., explicitly disclose method step of hybridization comprising contacting a polynucleotide [0061-0064]. Since claimed method is not drawn to a specific oligonucleotide as a probe for the hybridization, the method of Hopkins et al., would detect the nucleotide sequence having at least 95% identity to the sequence of SEQ ID NO: 43 or its full complement (page 586, col 2) and would anticipate the claimed method.

For this rejection the preamble of diagnosing cancer or breast cancer in patients does not limit the claims because the only active steps in these claims are contacting the nucleotide, comparing or determining the levels of the expression of gene product. The methods of Hopkins et al., disclose the method step of comparing or determining the levels of the claimed gene product in the patient samples compared to the normal samples, therefore, the reference teaches each and every limitation of the claimed method. For this rejection, the phrase "wherein, an increase of at least 50%, 100%, 150%, or 200% etc. from the levels of the mRNA in the breast patients sample relative to normal control " recited in the claims are not considered as an active method step. The wherein clause is interpreted as a mental step.

Art Unit: 1643

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 (a) are summarized as follows:

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 90-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Hopkins et al., (US Application Publication, 2002/0137077, filing 10/25/2001) in view of Martensen et al., (Eur. J. Biochem. vol 248, page 583-591, 1997) and Fodor et al., (US Patent No.5871928, issued 1999).

The claims are drawn to a method of diagnosing a breast cancer by contacting a polynucleotide that hybridizes under stringent condition to a nucleotide from a sample of breast cancer, wherein the hybridization is at 60°C or 50°C and 5XSSC.

The teaching of Hopkins et al., is set forth as in the 102 rejection above. Hopkins et al., also disclose method of hybridization comprising contacting a polynucleotide under stringent hybridization condition at 60 °C in 5XSSC [0064].

Hopkins et al., do not teach the nucleic acids from the patients with breast cancer and the hybridization of the polynucleotide under at 50°C in 5XSSC.

Art Unit: 1643

The teaching of Martensen et al., is set forth above, that is a method for detecting the differential gene expression of VLDLRs encoded by the mRNA of SEQ ID NO: 43 in the cell lines and breast carcinoma tissue samples compared to the normal cells or tissues (figure 1 and 5, page 585-6).

Fodor et al., teach that nucleotide hybridization would often be used, at about 45 °C or even high as about 50 °C or 60 °C (bridging col 49-50).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to optimize the hybridization condition and determine the expression of nucleotide sequence of SEQ ID NO: 43 or its variants in the samples from breast cancer cells or tissues. One of ordinary skill in the art at the time the invention was made would have been motivated to apply the teaching of Martensen et al., to the method of Hopkins et al., in order to benefit the breast cancer diagnosis because Martensen et al., teach the only increase expression of VLDLR-II in the breast cancer cell and tissues. One of ordinary skill in the art at the time the invention was made would have been further motivated to apply the teaching of Fodor et al., on the high stringent hybridization condition to the method of Hopkins et al., in order to screen the expression of entire, partial, or homologous of the gene product of SEQ IF NO: 43 because Fodor et al., suggest that the specific hybridization condition will be selected to correspond to a discriminatory condition (col 50, line 47+). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings to determine the levels of gene product of SEQ ID NO: 43 or its homologous at different hybridization condition because Hopkins et al., and Martensen et al., in combination have shown a method for detecting the gene product in breast cancer and Fodor et al., have shown the hybridization could be at 50°C or even higher. Therefore, the references in combination teach every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

For this rejection, the phrase "wherein, an increased levels of duplex of nucleotides from the patient samples relative to normal control indicates that the patient has breast cancer " recited in the claims are not considered as an active method step. The wherein clause is interpreted as a mental step.

Art Unit: 1643

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,
Examiner
Art Unit 1642

LY

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643